mTOR signaling regulates the morphology and migration of outer radial glia in developing human cortex.

Journal: Elife

Publication Year: 2020

Authors: Madeline G Andrews, Lakshmi Subramanian, Arnold R Kriegstein

PubMed link: 32876565

Funding Grants: Center of Excellence for Stem Cell Genomics - Stanford

Public Summary:

Scientific Abstract:
Outer radial glial (oRG) cells are a population of neural stem cells prevalent in the developing human cortex that contribute to its cellular diversity and evolutionary expansion. The mammalian Target of Rapamycin (mTOR) signaling pathway is active in human oRG cells. Mutations in mTOR pathway genes are linked to a variety of neurodevelopmental disorders and malformations of cortical development. We find that dysregulation of mTOR signaling specifically affects oRG cells, but not other progenitor types, by changing the actin cytoskeleton through the activity of the Rho-GTPase, CDC42. These effects change oRG cellular morphology, migration, and mitotic behavior, but do not affect proliferation or cell fate. Thus, mTOR signaling can regulate the architecture of the developing human cortex by maintaining the cytoskeletal organization of oRG cells and the radial glia scaffold. Our study provides insight into how mTOR dysregulation may contribute to neurodevelopmental disease.